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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,914	TRIPET ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,37 and 39-44* is/are pending in the application.

4a) Of the above claim(s) *7,12,14-18,24-28 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-11,13,19-23,37 and 40-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/17/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *attachements*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, and HR-C peptide analog SEQ ID NO: 67, in the reply filed on February 25, 2009, is acknowledged.

2. Applicant traverses the restriction on the ground(s) that the inclusion of the subject matter of nucleic acids (Group II) which correspond to elected peptides would not impose an undue search burden. However, this argument is found not persuasive. This is a 371 case. Under PCT Rule 13.2, the inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1. Therefore, the restriction groupings are proper. Search and examination of different inventions would impose an undue search burden on the Office.

3. Applicant traverses the species election on the ground(s) that many of the allegedly distinct peptides do share a common property or activity. This argument is not found persuasive, either. The claims include 77 peptides with SEQ ID NOs. Despite their common origin from the SARS spike protein, Applicant has not specifically pointed out what common property or activity these peptides share, and what common structural feature they share as a source of their common activity. If applicant is willing to admit that all 77 peptides are not patentably distinct, then the various peptides can be rejoined. Furthermore, search and examination of 77 peptide sequences presented in the instant claims spontaneously constitutes a serious burden to the Office. By examining Applicant's preferred species first and then genus is a logical approach to search and examine the entire application efficiently (see MPEP 803.02). The requirement is still deemed proper and is therefore made FINAL.

4. Accordingly, Claims 1-28, 37 and 39-44 are pending. Claims 7, 12, 14-18, 24-28 and 39

are withdrawn as non-elected. Claims 1-6, 8-11, 13, 19-23, 37 and 40-44 are considered in this Office action.

Priority

5. Applicant's claim for domestic priority of the provisional application 60/544,410 under 35 U.S.C. 119(e) is acknowledged. However, a review of 60/544,410 indicates, while providing support for the generic Claims 1-5, 9, 11 and 19-22 in the priority document, 60/544,410 fails to provide adequate support under 35 U.S.C. 112 for the peptide SEQ ID NO: 67 of Claims 6, 8, 10, 13, 23, 37 and 40-44 of this application. Therefore, the priority date of Claims 1-5, 9, 11 and 19-22 is deemed to be February 12, 2004, the filing date of provisional application 60/544,410. The priority date of Claims 6, 8, 10, 13, 23, 37 and 40-44 is deemed to be February 14, 2005, the filing date of PCT/US05/04408.

Specification

6. The specification is objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific amino acid sequences comprising four or more amino acids and ten or more nucleic acids in the specification. Specific examples within the specification that do not comply with the sequence rules are found Figures. Applicant is required to append a SEQ ID NO: to any unidentified sequence within the disclosure that is applicable to the rule. See 37 CFR § 1.821 (a)-(d) and MPEP § 2422.

Claim Objections

7. Claim 13 lacks a transitional phrase. It is not clear said HR peptide is "comprising" or "consisting of" HR-C4a. For the purpose of examination, the claim read on "wherein said HR peptide comprising HR-C4a of SEQ ID NO: 67". Appropriate correction is required for clarity.

Claim Rejections - 35 USC § 112, second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "a transition midpoint temperature" is not defined by the specification. It is not clear if the term "a transition midpoint temperature" is equivalent to the standard term ½ melting temperature (*Tm*). Moreover, Claims 19-22 are incomplete because of the omission of essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. According to Para [0129] of the specification, the term "a transition midpoint temperature" was used to describe the temperature where a disulfide bridged **complex** of HR-N and HR-C peptides is separated (melted). However, Claims 19-23 are directed to either HR-N or HR-C peptide, not a complex. It is not clear how to determine "a transition midpoint temperature" of a single peptide. Appropriate correction is required.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-6, 9, 10, 19-23 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Rottier *et al* US 20040071709, filing date April 14, 2003).

12. Rottier teaches a 49-mer HR-C peptide of SEQ ID NO: 27, which is derived from SARS-CoV (Tort2 strain). The HR-C peptide of SEQ ID NO: 27 of the prior art comprises a continuous strand of 14 amino acids of SEQ ID NO: 67 of the instant claims, see sequence alignment below (also the attachment).

```
Qy      1 DISGINASVVNIQKEIDRLNEVIKNLNESLIDLQEL 36 SEQ ID NO:67
          |||||||||||||||||||| ||||||||||||
Db      7 DISGINASVVNIQKEIDRLNEVAKNLNESLIDLQEL 42 SEQ ID NO:27,
                                                  Rottier
```

Rottier teaches that S proteins of SARS-CoV, other human coronaviruses and mouse hepatitis virus (MHV) also possess an alpha-helical trimeric conformation, see e.g. [0051][0057] and [0060]. HR2 peptides of coronavirus, including SARS-CoV, can inhibit anti-parallel coiled coil formation of a coronavirus spike protein by decreasing the contact between heptad repeat regions of the protein, See e.g. [0019] [0021]. Therefore, they are "powerful antivirals for the therapy of coronavirus-induced diseases both in animals and man" See Para [0061]. Rottier exemplifies that HR peptides from MHV-A59 strongly inhibits viral entry and syncytium formation, see

[0091][0092]. In view of these teachings, Claims 1-6, 9, 10, 19-23 and 37 are anticipated by Rottier.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering the patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of their obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-6, 8-11, 13, 19-23, 37 and 40-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rottier *et al* US 2004/0071709, in view of Kliger (BMC Microbiology, 2003, 3:20, p. 1-7.).

Note: Definition of "heptad repeat (HR)": The specification does not explicitly define "heptad repeat", but provided the following description about "heptad repeat unit" in Para [0083]:

[0083]The positions of a heptad repeat unit are denoted as (abcdefg)n, where n is a repeat number. The residues at the a and d positions (of the heptad repeat positions denoted (abcdefg)n of HR-C then pack into grooves formed by the residues at the a, d, e and g positions of the HR-N

core coiled-coil to complete the 6-stranded alpha-helical bundle structure also termed "trimer of hairpins" or "trimer of dimers".

Followings are plain definitions of "heptad repeat" in the art, which provide more structural description of the "heptad repeat" motif:

"Heptad repeat is a type of tandem repeat sequence in which a group of seven amino acids occurs many times in a protein sequence. (from online medical dictionary from mondofacto, see the attachment to this Office action).

"The **heptad repeat** is an example of a structure motif which consists of a repeating pattern of amino acids:

a b c d e f g
H P P **H** P P P

where **H** represents hydrophobic residues and P represents polar (and therefore hydrophilic) residues. The positions of the heptad repeat are commonly denoted by the lower case letters *a* through *g*. These motifs are the basis for most coiled coils and in particular, leucine zippers, which predominantly have leucine in the *d* position of the heptad repeat." (from Wikipedia, See the attachment to the Office action).

15. The relevance of Rottier is set froth *supra*. Moreover, Rottier teaches HR2 sequence homology between HR2 of SARS-CoV and those of other coronaviruses, see sequence alignment in Fig. 10a. It is noted that, unlike C-HRs of other S proteins coronavirus, C-HR segment of native SARS S protein has amino acid A (Alanine) rather than I (Isoleucine) at the position corresponding to residue 23 of SEQ ID NO: 27, see Fig. 10A. (Also see the attached Fig. 10A, where A/I position is indicated).

16. Rottier does not explicitly cite the instant HR-C4a **analog** of SEQ ID NO: 67, which contains substitution of amino acid I for native amino acid A in the position corresponding to residue 23 of SEQ ID NO: 27 (native HR2 of SARS-CoV).

17. Kliger teaches C-HR (*C*-terminal HR), "ISGINASVVNIQKEIDRLNEVAKNLNESLIDLQEL", a Leucine/Isoleucine (L/I) heptad

repeat, appears on the residues 1151-1185 of SARS S protein, see e.g. last Para, left col. p. 4, and Figure 3b. In Figure 3, Kliger shows that the helical wheel of C-HR, which consists of seven corners, corresponding to the fit of **seven amino acid residues into every two helical turns**, wherein the residues L and I, which are key amino acids for forming the HR helix motif, are labeled in bold (See Fig. 3b and description).

18. In the recently decided case of *KSR International Co. v. Teleflex Inc.* (82 U.S.P.Q. 2d1385, 2007), the Supreme Court provided a number of bases on which a claimed invention may be found obvious. In particular, "When there is a design need or market pressure to solve a problem and there are a finite number of identified predictable potential solutions, **a person of ordinary skill has good reason to pursue the known potential options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense**" (Emphasis added).

19. In the present case, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make HR-C4a analog of SEQ ID NO: 67, by substituting amino acid I for native amino acid A of the native HR segment, in order to make a more stable helix structure.

```
 H  H   H  H   H  H   H  H   H  H  H
                        abcdefg
DISGINASVVNIQKEIDRLNEVIKNLNESLIDLQEL 36      SEQ ID NO:67
DISGINASVVNIQKEIDRLNEVAKNLNESLIDLQEL 42      SEQ ID NO:27, Rottier
 ISGINASVVNIQKEIDRLNEVAKNLNESLIDLQEL 35      native C-HR, Kliger
 H  H   H  H   H  H      H   H  H  H
 *      *      *      *      *     *
```

Where * indicate seven amino acid residues into every two helical turns; H represents hydrophobic residues; and "***I***" and "***A***" in bold italic are residues focused in the discussion, see the text.

Examples of hydrophobic residues are: **L** (Leucine), **I** (Isoleucine), **P** (phenylalanine) and **V** (Valine).

The sequence comparison above shows that native HR segment of SARS, which comprises residue A, rather than a hydrophobic residue, see SEQ ID NO:27, Rottier and native C-HR, Kliger in the Figure above. So native HR segment of SARS would form a less ideal alpha-helical trimeric conformation of a HR peptide, according to the standard structure motif of HR, see Definition of "heptad repeat (HR)", in Para 13 above. One skilled in the art would have been motivated to modify the native HR peptide by replacing I for native residue A, resulting in analog SEQ ID NO: 67, because improved stability of an alpha-helical trimeric conformation of a HR peptide is a desirable characteristic, and also given the knowledge that HRs of all other coronaviruses are comprised of I, rather than A, at the position corresponding to position 23 of SEQ ID NO: 27, as taught by Rottier, See attached Rottier, Fig. 10A. Since standard HR structure features were well characterized at the time the invention was made, "a person of ordinary skill has good reason to pursue the known potential options (replacing I for native A) within his or her technical grasp". Considering the similarity in structure and function of inhibitory HR peptides in the prior art, it can be concluded that there was a reasonable expectation of success in obtaining HRs analog, like SEQ ID NO: 67. The invention as a whole is therefore *prima facie* obvious, absent unexpected results.

Remarks

20. No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Examiner, Art Unit 1648